

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) An isolated anti-human tenascin monoclonal antibody or a proteolytic ~~fragment~~ ~~fragments~~ thereof, comprising a light chain variable region of SEQ ID NO:2 and a heavy chain variable region of SEQ ID NO:4, wherein said light chain variable region and said heavy chain variable region are capable of binding to an antigenic epitope within the A₍₁₋₄₎-D region of human tenascin.

2. (Currently Amended) The fragment ~~fragments~~ of the antibody according to claim 1, further containing additional markers and diagnostic agents.

3-7. (Cancelled).

8. (Currently Amended) The antibody or the fragment ~~proteolytic fragments~~ thereof according to claim 1, wherein said antibody or said fragment ~~proteolytic fragments~~ thereof are biotinylated.

9.-11. (Cancelled).

12. (Currently Amended) An isolated antibody or a fragment ~~fragments~~ thereof coded for by the nucleotide sequences SEQ ID NO:1 and SEQ ID NO:3.

13.-14. (Cancelled).

15. (Previously Presented) Hybridoma producing the antibody according to claim 1, deposited at the Centro di Biotecnologie Avanzate, Largo Rossana Benzi 10 Genoa – Italy on 12 November 2003 in accordance with the provisions of the Budapest Treaty, with the accession number PD03003.

16. (Previously Presented) Process for the preparation of the antibody according to

claim 1 comprising

- a) immunizing an animal with the A₍₁₋₄₎-D fragment of human tenascin;
- b) fusing somatic spleen cells of said animal with myeloma cells not producing immunoglobulins;
- c) selecting the monoclonal antibody.

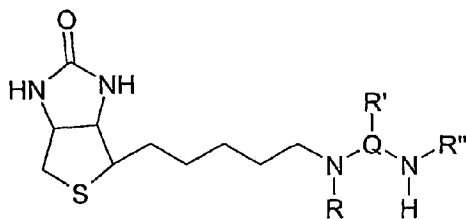
17.-20. (Cancelled).

21. (Currently Amended) A pharmaceutical or diagnostic composition ~~compositions~~ containing an antibody or a proteolytic fragment ~~fragments~~ thereof according to claim 1, with at least one pharmaceutically acceptable vehicle or excipient.

22. (Currently Amended) A kit for systemic radioimmunotherapy consisting of 5 vials: wherein vial 1 contains the antibody or the proteolytic fragment ~~fragments~~ thereof according to claim 1; vial 2 contains avidin; vial 3 contains streptavidin; vial 4 contains biotinylated human albumin; and vial 5 contains biotin DOTA.

23. (Currently Amended) A kit for locoregional radioimmunotherapy consisting of 3 vials; wherein vial 1 contains the antibody or the proteolytic fragment ~~fragments~~ thereof according to claim 1, vial 2 contains avidin; and vial 3 contains biotin DOTA.

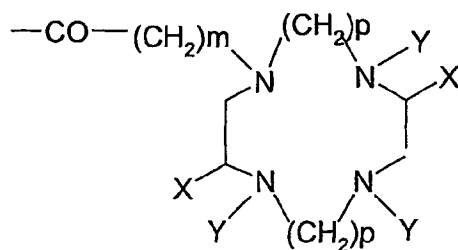
24. (Currently Amended) The kit according to claim 22 wherein said biotin DOTA in vial 5 is the formula (I) compound



(I)

in which Q is a $-(CH_2)_n-$ group, where n is a whole number from 4 to 12, in which case R' is not present, or Q is selected from the group consisting of $-(CH_2)_a-CH(R')_b-(CH_2)_b-$, where a and b are independently whole numbers from 0 to n, wherein n is as defined above, R' is as defined here below, or Q is cyclohexyl, phenyl, in which case R' is a substituted on the cyclohexyl or phenyl ring;

R is hydrogen or $-\Lambda$ where $-\Lambda$ is a formula (II) macrocycle



(II)

where the various Y's which may be the same or different, are selected from the group consisting of hydrogen, straight or branched C_1 - C_4 alkyl, $-(CH_2)_m-COOH$, where m is a whole number from 1 to 3, X is hydrogen, or the group $-CH_2-U$, where U is selected from the group consisting of methyl, ethyl, and p-aminophenyl, or X is the group $-(CHW)_o-Z$, where o is a whole number from 1 to 5, W is hydrogen, methyl or ethyl, Z is a 5- or 6- member heterocyclic group containing one or more heteroatoms selected from O, N- R_1 , where R_1 is hydrogen or straight or branched C_1 - C_4 alkyl, and S; or Z is selected from the group consisting of $-NH_2$, $-NH-C(=NH)-NH_2$, or $-S-R_2$, where R_2 is straight or branched C_1 - C_4 alkyl;

p is the number 2 or 3;

R' is selected from the group consisting of hydrogen, straight or branched C₁-C₄ alkyl, -(CH₂)_q-T, in which T is selected from the group consisting of -S-CH₃, -OH, -COOH, and q is the number 1 or 2;

R'' has the same meanings as R', upon the following conditions: if R is -Λ, R'' is hydrogen, if R is hydrogen, R'' is -Λ, or R and R'' are, respectively -(CH₂)_r-Λ (for R), where r is a whole number from 4 to 12, and -Λ (for R'), Q being a -(CH₂)_n- group, where n is a whole number from 4 to 12.

25. (Currently Amended) The kit according to claim 22, in which vial 3 contains an avidin dimer in which two avidin molecules are bound via the -NH₂ groups by means of suberate.

26. (Currently Amended) The kit according to claim 22, in which said vial 3 contains an avidin dimer in which two avidin molecules are bound via the -COOH groups by means of polyethylene glycol with a molecular weight of 3,400.

27. (Currently Amended) The kit according to claim 22, in which the antibody or the proteolytic fragment ~~fragments~~ thereof are combined with other anti-tenascin antibodies.

28. (Currently Amended) The kit according to claim 22, wherein the antibody or the proteolytic fragment ~~fragments~~ thereof are combined with other tumor-specific antibodies.

29. (Cancelled).

30. (Currently Amended) Container containing the antibody or the proteolytic fragment ~~fragments~~ thereof according to claim 1.

31.-32. (Cancelled).

33. (Currently Amended) Combination comprising the antibody or the proteolytic fragment ~~fragments~~ thereof according to claim 1, and a second tenascin-specific antibody.

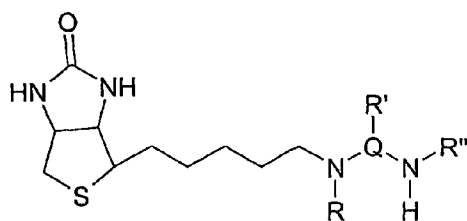
34. (Cancelled).

35. (Currently Amended) An isolated murine anti-human tenascin monoclonal antibody or a proteolytic fragment ~~fragments~~ thereof comprising a light chain variable region of SEQ ID NO:2 and a heavy chain variable region of SEQ ID NO:4, wherein said light chain variable region and said heavy chain variable region are capable of binding to an antigenic epitope within the A₍₁₋₄₎-D region of human tenascin.

36. (Currently Amended) ~~Recombinant derivative of the~~ An antibody or a fragment thereof according to claim 35 comprising a human constant region.

37. (Currently Amended) The kit according to claim 23 wherein in which said biotin DOTA

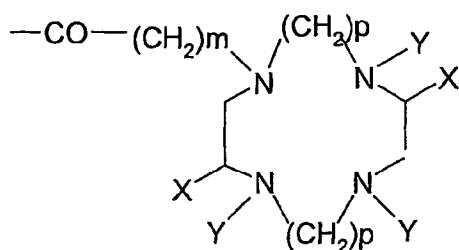
in vial 2 is the formula (I) compound



(I)

in which Q is a $-(CH_2)_n-$ group, where n is a whole number from 4 to 12, in which case R' is not present, or Q is selected from the group consisting of $-(CH_2)_a-CH(R')_b-(CH_2)_b-$, where a and b are independently whole numbers from 0 to n, wherein n is as defined above, R' is as defined here below, or Q is cyclohexyl, phenyl, in which case R' is a substituted on the cyclohexyl or phenyl ring;

R is hydrogen or $-\Lambda$ where $-\Lambda$ is a formula (II) macrocycle



(II)

where the various Y's which may be the same or different, are selected from the group consisting of hydrogen, straight or branched C₁-C₄ alkyl, -(CH₂)_m-COOH, where m is a whole number from 1 to 3, X is hydrogen, or the group -CH₂-U, where U is selected from the group consisting of methyl, ethyl, and p-aminophenyl, or X is the group -(CHW)_o-Z, where o is a whole number from 1 to 5, W is hydrogen, methyl or ethyl, Z is a 5- or 6- member heterocyclic group containing one or more heteroatoms selected from O, N-R₁, where R₁ is hydrogen or straight or branched C₁-C₄ alkyl, and S; or Z is selected from the group consisting of -NH₂, -NH-C(=NH)-NH₂, or -S-R₂, where R₂ is straight or branched C₁-C₄ alkyl;

p is the number 2 or 3;

R' is selected from the group consisting of hydrogen, straight or branched C₁-C₄ alkyl, -(CH₂)_q-T, in which T is selected from the group consisting of -S-CH₃, -OH, -COOH, and q is the number 1 or 2;

R'' has the same meanings as R', upon the following conditions: if R is -Λ, R'' is hydrogen, if R is hydrogen, R'' is -Λ, or R and R'' are, respectively -(CH₂)_r-Λ (for R), where r is a whole number from 4 to 12, and -Λ (for R'), Q being a -(CH₂)_n- group, where n is a whole number from 4 to 12.